Pediatric Assessment in Drug Development and Regulatory Approval in Japan

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Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the Pharmaceuticals and Medical Devices Agency.
Agenda

- Regulations and NDA review of Pediatric Drugs in Japan
- Pediatric Drug Development in Japan
- Future Challenges
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Pediatric Regulations in Japan

- There is no regulation mandating pediatric studies.
- ICH-E11
- Several frameworks to enhance pediatric drug development has been implemented.
  - Extension of exclusive period
  - Council for unapproved drugs/indications
  - National network for pediatric clinical studies
  - Pediatric Drugs WG in PMDA
  - Priority for scientific advice by PMDA
Post-marketing Review of New Drugs

- Post-marketing safety and efficacy for new drugs are reviewed a certain period after the approval for marketing authorization.
- Generic drugs are not approved for the marketing prior to the post-marketing review of new drugs. → Similar to the exclusive sales period for new drugs.

<table>
<thead>
<tr>
<th>Terms for post-marketing review</th>
<th>10 years</th>
<th>8 years</th>
<th>4 years</th>
<th>4-6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Orphan Drugs</td>
<td>• Drugs with new active ingredients</td>
<td>• New combination drugs</td>
<td>• Drugs with a new indications</td>
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<tr>
<td></td>
<td>• Drugs required long-term pharmacoepidemiological study</td>
<td></td>
<td>• Drugs with a new route of administration</td>
<td>• Drugs with a new dosage</td>
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IND for pediatric study

The term can be extended up to 10 years
Council for Unapproved Drugs/indications

- Identifies highly-needed unapproved drugs/indications, including for pediatrics, which are widely used in at least one of the 6 countries (Australia, Canada, France, Germany, UK, US).
- MHLW requests pharmaceutical industries to submit the NDA of designated drugs/indications raising the product price as a reward.
- PMDA reviews the NDA on fast track and accept public knowledge as the basis for the approval.
  - Large experience of clinical use and clinical data submitted to the regulatory authority in one of the 6 areas are available
  - Described in the medical textbooks or guidance documents
- 157 products/indications have been approved until Dec. 2015 and 29 of them are pediatric dosage or indications.
Pediatric Drugs WG in PMDA

- One of the projects across multi-offices in PMDA
- Established in November 2011

**International Collaborations**
- FDA
- European Medicines Agency
- Health Canada
- TGA

**External Communications**
- Discuss pediatric issues with domestic stakeholders

**Analyses**
- Members from Offices of New Drug, Office of Safety, Office of Regulatory Science.
- Analyze and identify pediatric issues raised in past reviews and consultations

**Internal Communications**
NDA Review and Scientific Advice for Pediatric Drugs

Pediatric Drugs WG

All Pediatricians in PMDA are enrolled

Pediatrician(s) participates in NDA review and Scientific Advise for pediatric drugs

Review Team

Encourage sponsors in pediatric development at Scientific Advice meeting for the drug which can be used for children
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New Drug Approval

- **Total**:
  - 2009: 103
  - 2010: 114
  - 2011: 131
  - 2012: 133
  - 2013: 128
  - 2014: 119

- **Paediatric**:
  - 2009: 19
  - 2010: 26
  - 2011: 35
  - 2012: 44
  - 2013: 38
  - 2014: 39

**Ratio (%):**
- 2009: 18.4%
- 2010: 22.8%
- 2011: 26.7%
- 2012: 33.1%
- 2013: 29.7%
- 2014: 32.8%

* J-FY is from April to March next year.
Products Approved with Pediatric Indication and Dosage

* J-FY is from April to March next year.
Global Pediatric Clinical Trials

Source: http://ClinicalTrials.gov

As of Mar 4th, 2016

Search Term: pediatric, Funder type: industry

Include only open studies, exclude studies with unknown status
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Advanced workflow of review/consultation from Oct 2016

- Analysis by PMDA
  - Giving additional scientific value to submitted data

- Data Accumulation
  - e-Submission of study data

- Database
  - Sophisticated Consultation
    - More evidence-based consultation

- Sophisticated review
  - Each reviewer utilizes innovative assessment techniques

- Cross-Products Analysis
  - Advanced evaluation methods
  - Active utilization of Modeling & Simulation
    - Disease model
    - Objective B/R assessment
    - Identifying AE-related factors etc.

- Cooperative with Academia

- Practical use of Innovative Medical Products
  - More rational & effective evaluation process for regulatory decision

- More effective and high quality Review
  - More predictable efficacy/safety after approval
  - Reduction of applicant’s work load
  - More scientific regulatory decision

- More efficient and Successful Development
  - Epoch-making proposal leading the world
  - Proactive publication of guideline
A Discussion Framework in PMDA on Modeling and Simulation Issues

Objectives

- Discuss M&S issues in scientific advice and NDA review
- Share the knowledge and experiences across review teams
- International collaboration
Future Development of Guidelines

The Research group consist of experts from PMDA, academia and industries are drafting following regulatory documents on utilization of modeling and simulation in clinical development including drugs for pediatric and unmet medical needs:

- Guideline on Population Pharmacokinetics and Pharmacodynamics Analyses (draft)
  - Updating the general guidance on PK study published in 2003 to establish best practices/guidance in population PKPD analysis
  - Draft guideline were published in December, 2015.
  - Final guideline will be published in 2016.

- Guideline on D-E-R Relationships and Modeling
  - Under discussion
  - Drug development strategy and clinical study plan for rare disease and pediatric will be mentioned
  - Draft guideline is expected to be published in J-FY 2017?

- Point to consider on Cross-Product Analysis
  - Going to be discussed on specific therapeutic areas
  - General considerations will be shown
Thank you for your attention

PMDA strongly supports pediatric drug development!

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